



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of :

Giorgio Attardo

Group Art Unit: 1616

Serial No.: 09/976,249

Examiner: Unassigned

Filed: October 15, 2001

For: DIOXOLANE ANALOGS FOR IMPROVED INTER-CELLULAR DELIVERY

**PRELIMINARY AMENDMENT**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Prior to initial examination, please amend the above-identified application as follows:

**IN THE ABSTRACT:**

Please add the Abstract attached hereto on a separate sheet.

**IN THE CLAIMS:**

Please amend the claims as follows:

--29. (Amended) A method according to claim 1, wherein said cancer is prostate cancer, colon cancer, lung cancer, melanoma, ovarian cancer, renal cancer, breast cancer, lymphoma, pancreatic cancer or bladder cancer.

30. (Amended) A method according to claim 3, wherein said cancer is leukemia.

31. A method according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>3</sub>, or R<sub>4</sub> is piperazinyl, piperidinyl, morpholinyl, pyrrolidinyl, adamantyl or quinuclidinyl.

**PHARMA-123**

32. (Amended) A method according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>3</sub> or R<sub>4</sub> is acetyl, propionyl, butyryl, valeryl, caprioic, caprylic, capric, lauric, myristic, palmitic, stearic, oleic, linoleic, or linolenic.

33. (Amended) A method according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>3</sub> or R<sub>4</sub> is cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, phenyl, naphthyl or biphenyl.

34. (Amended) A method according to claim 1, wherein at least one of R<sub>1</sub>, R<sub>3</sub> or R<sub>4</sub> contains a heterocyclic group selected from the following group:

furyl, thiophenyl, pyrrolyl, imidazolyl, pyrazoyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyridyl, pyrimidinyl, triazolyl, tetrazolyl, oxadiazolyl, thiadiazolyl, thiopyranyl, pyrazinyl, benzofuryl, benzothiophenyl, indolyl, benzimidazolyl, benzopyrazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl, benzisothiazolyl, benzoxadiazolyl, quinolinyl, isoquinolinyl, carbazolyl, acridinyl, cinnolinyl and quinazolinyl.

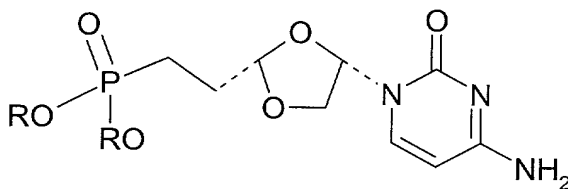
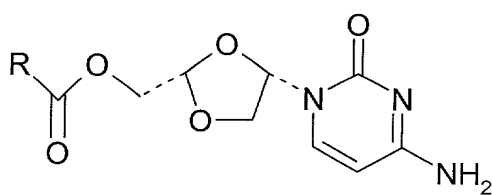
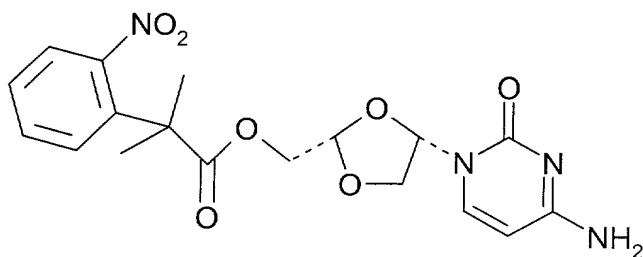
35. (Amended) A method according to claim 1, wherein said compound is administered at least daily for a period of 2 to 10 days every 2 to 5 weeks.

36. (Amended) A method according to claim 1, wherein said compound is administered at least daily for a period of 2 to 10 days every 3 to 4 weeks.

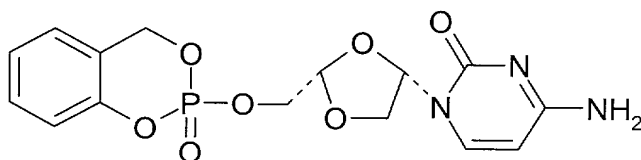
37. (Amended) A method according to claim 1, wherein said compound is administered at least daily for 3 to 7 days every 2 to 5 weeks.

38. (Amended) A method according to claim 1, wherein said compound is administered at least daily 4 to 6 days every 2 to 5 weeks.

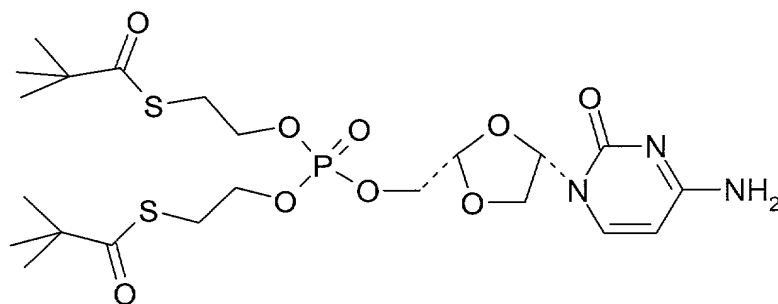
44. (Amended) A method according to claim 1, wherein the compound is of the formulas



45. (Amended) A method according to claim 1, wherein the compound is of the formula



46. (Amended) A method according to claim 1, wherein the compound is of the formula



47. A method according to claim 1, wherein the compound is selected from  
4-HEXYL-BENZOIC ACID 4-(4-AMINO-2-OXO-2H-PYRIMIDIN-1-YL)-  
[1,3]DIOXOLAN-2-YLMETHYL ESTER;

8-PHENYL-OCTANOIC ACID [1-(2-HYDROXYMETHYL-[1,3]DIOXOLAN-4-YL)-  
2-OXO-1,2-DIHYDRO-PYRIMIDIN-4-YL]-AMIDE;

8-PHENYL-OCTANOIC ACID 4-(4-AMINO-2-OXO-2H-PYRIMIDIN-1-YL)-[1,3]  
DIOXOLAN-2-YLMETHYL ESTER;

4-PENTYL-BICYCLO[2.2.2]OCTANE-1-CARBOXYLIC ACID 4-(4-AMINO-2-OXO-  
2H-PYRIMIDIN-1-YL)-[1,3]DIOXOLAN-2-YLMETHYL ESTER;

4-PENTYL-CYCLOHEXANECARBOXYLIC ACID 4-(4-AMINO-2-OXO-2H-  
PYRIMIDIN-1-YL)-[1,3]DIOXOLAN-2-YLMETHYL ESTER;

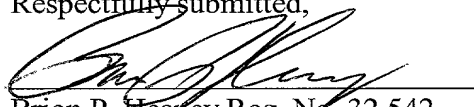
or mixtures thereof.--

**REMARKS**

The amendments to the claims are made to delete multiple dependence and to correct obvious typographical errors and eliminate superfluous language. It is respectfully submitted that no new subject matter has been added and entry of the amendment is respectfully requested.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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Attorney Docket No.: PHARMA-123

Date: January 16, 2002

**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

The claims have been amended as follows:

29. (Amended) A method according to ~~any one of claims~~ claim 1-28, wherein said cancer is prostate cancer, colon cancer, lung cancer, melanoma, ovarian cancer, renal cancer, breast cancer, lymphoma, pancreatic cancer or bladder cancer.

30. (Amended) A method according to ~~any one of claims~~ claim 3-28, wherein said cancer is leukemia.

31. (Amended) A method according to ~~any one of claims~~ claim 1-28, wherein at least one of R<sub>1</sub>, R<sub>3</sub>, or R<sub>4</sub> is piperazinyl, piperidinyl, morpholinyl, pyrrolidinyl, adamantyl or quinuclidinyl.

32. (Amended) A method according to ~~any one of claims~~ claim 1-28, wherein at least one of R<sub>1</sub>, R<sub>3</sub> or R<sub>4</sub> is acetyl, propionyl, butyryl, valeryl, caprioic, caprylic, capric, lauric, myristic, palmitic, stearic, oleic, linoleic, or linolenic.

33. (Amended) A method according to ~~any one of claims~~ claim 1-28, wherein at least one of R<sub>1</sub>, R<sub>3</sub> or R<sub>4</sub> is cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, phenyl, naphthyl or biphenyl.

34. (Amended) A method according to ~~any one of claims~~ claim 1-28, wherein at least one of R<sub>1</sub>, R<sub>3</sub> or R<sub>4</sub> contains a heterocyclic group selected from the following group:

furyl, thiophenyl, pyrrolyl, imidazolyl, pyrazoyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyridyl, pyrimidinyl, triazolyl, tetrazolyl, oxadiazolyl ~~oxadrazolyl~~, thiadiazolyl, thiopyranyl, pyrazinyl, benzofuryl, benzothiophenyl, indolyl, benzimidazolyl, benzopyrazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl ~~benzothiezolyl~~, benzisothiazolyl,

benzoxadiazolyl, quinolinyl, isoquinolinyl, carbazolyl, acridinyl, cinnolinyl and quinazolinyl.

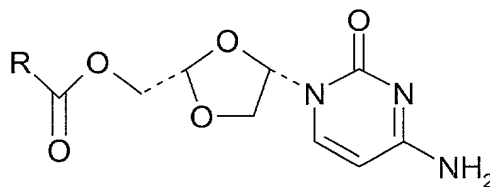
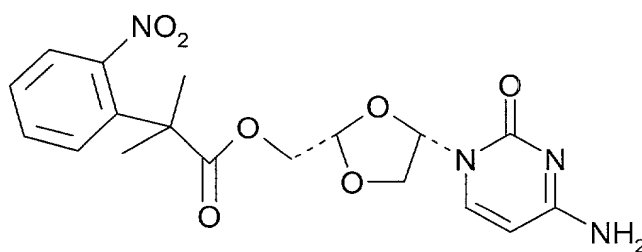
35. (Amended) A method according to ~~any one of claims~~ claim 1-28, wherein said compound is administered at least daily for a period of 2 to 10 days every 2 to 5 weeks.

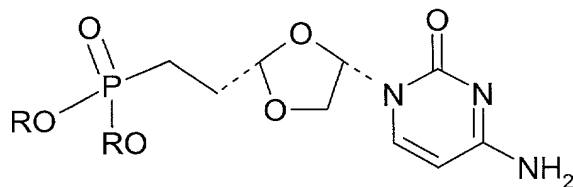
36. (Amended) A method according to ~~any one of claims~~ claim 1-28, wherein said compound is administered at least daily for a period of 2 to 10 days every 3 to 4 weeks.

37. (Amended) A method according to ~~any one of claims~~ claim 1-28, wherein said compound is administered at least daily for 3 to 7 days every 2 to 5 weeks.

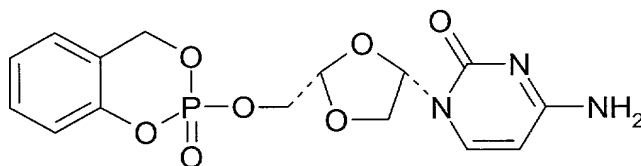
38. (Amended) A method according to ~~any one of claims~~ claim 1-28, wherein said compound is administered at least daily 4 to 6 days every 2 to 5 weeks.

44. (Amended) A method according to ~~any one of claims~~ claim 1-28, wherein the compound is of the formulas

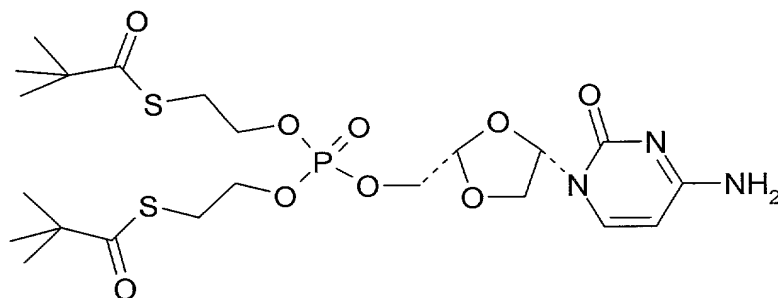




45. (Amended) A method according to ~~any one of claims~~ claim 1 to 28, wherein the compound is of the formula



46. (Amended) A method according to ~~any one of claims~~ claim 1 to 28, wherein the compound is of the formula





46 47. (Amended) A method according to ~~any one of claims~~ claim 1 to 28, wherein the compound is selected from

4-HEXYL-BENZOIC ACID 4-(4-AMINO-2-OXO-2H-PYRIMIDIN-1-YL)-  
[1,3]DIOXOLAN-2-YLMETHYL ESTER (~~No. 191~~);

8-PHENYL-OCTANOIC ACID [1-(2-HYDROXYMETHYL-[1,3]DIOXOLAN-4-YL)-  
2-OXO-1,2-DIHYDRO-PYRIMIDIN-4-YL]-AMIDE (~~No. 197~~);

8-PHENYL-OCTANOIC ACID 4-(4-AMINO-2-OXO-2H-PYRIMIDIN-1-YL)-[1,3]  
DIOXOLAN-2-YLMETHYL ESTER (~~No. 198~~);

4-PENTYL-BICYCLO[2.2.2]OCTANE-1-CARBOXYLIC ACID 4-(4-AMINO-2-OXO-  
2H-PYRIMIDIN-1-YL)-[1,3]DIOXOLAN-2-YLMETHYL ESTER (~~No. 211~~);

4-PENTYL-CYCLOHEXANECARBOXYLIC ACID 4-(4-AMINO-2-OXO-2H-  
PYRIMIDIN-1-YL)-[1,3]DIOXOLAN-2-YLMETHYL ESTER; (~~No. 240~~)

or mixtures thereof.